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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/768,080	01/23/2001	David A. Estell	GC527C3	2502

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EXAMINER	
SAUNDERS, DAVID A	

ART UNIT	PAPER NUMBER
1744	13

DATE MAILED: 01/07/2003

Please find below and or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
768,080	BASTELL et al
Examiner	**Group Art Unit**
SAUNDERS	

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 10/9/02.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 7-10, 14-15 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 7-10, 14-15 is/are rejected.

Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachm nt(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

Notice of Draftsperson's Patent Drawing Review, PTO-948

Other _____

Office Action Summary

Applicant's election with traverse of Group I (claims 7-10 and 14-15) in Paper No. 11(filed 10/9/02) is acknowledged. The traversal is on the ground(s) that there would be no additional burden to search for various proteins having greater immunogenicity along with those proteins having lesser immunogenicity. This is not found persuasive because the searches are divergent. For example proteins altered to have less immunogenicity would include proteases and lipases (e.g. in detergents), therapeutic proteins (e.g. antibodies, clotting factors, clot "busters"). One the other hand proteins altered to have greater immunogenicity would include vaccines. A disclosure of one would not show the other and would not suggest the other.

The requirement is still deemed proper and is therefore made FINAL.

Claims 7-10 and 14-15 and are being examined for the embodiment of variants that incur a reduced immunogenic response.

The disclosure is objected to because of the following informalities: at specification page 1, the Cross-Reference to Related Applications section fails to refer to several related applications, for which applicant has claimed benefit in the declaration.

At page 15, line 19 the applicant has referred to an "R factor" without providing the formula therefore, as was provided in earliest application 09/060,872.

Appropriate correction is required.

Claims 7 and 8 are objected to because of the following informalities: In claims 7 and 8 "a individual" should read as--an individual --. Appropriate correction is required.

Claims 8-10 and 14-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 8, line 5 "comprising said T-cell replaced with" is confusing. It is deemed that applicant intends insertion of – epitope – before "replaced".

In claim 8, last line "said replaced epitope" lacks antecedent basis. The above-indicated correction for line 5 would overcome this basis of rejection.

In claims 9 and 10 "said polypeptide of interest and said homologue combined" is unclear, because nothing in base claim 8 has been recited as "combined". Note, that the phrase could be understood as reciting that the variant has at least one (or two) less T-cell epitopes than the sum of the total number of epitopes of the polypeptide of interest and the total number of epitopes in the homolog. It is not believed that this is what applicant intends.

Claim 7 is rejected under 35 U.S.C. 102(b) as being anticipated by Carr (WO 98/52976), of record in IDS filed 2/8/00 for related application 09/500,135.

Carr shows modification of streptokinase by identifying T-cell epitopes therein and then modifying these epitopes by substitution of amino acid residues within these epitopes. See pages 4 and 35-38. With these modifications the kinase is less immunogenic. Applicant's claim 7 is considered anticipated.

I n another embodiment Carr discloses the modification of antibodies, such as monoclonal antibodies from a mouse, for use in humans. Within the V-region T-cell

epitopes are identified and altered by amino acid substitutions to eliminate these. In this manner, claim 7 is anticipated.

Carr also discloses that the mouse C-region can be replaced with a corresponding C-region from a human antibody. This C-region from the human source properly constitutes " a corresponding terminal portion of a homolog" of the mouse monoclonal antibody. Thus claim 8 is included in the rejection.

Claims 9-10 are included because replacing the whole of a mouse antibody C-region with a human C-region with a human C-region would be expected to eliminate multiple T-cell epitopes.

Applicant is referred to Carr at Pages 6-13, for example, for teachings of the modification of mouse antibodies to render such less immunogenic.

Claims 7-10 are rejected under 35 U.S.C. 102 (b) as being anticipated by Robinson et al. (5,500,362) in light of Carr et al.

Robinson et al. disclose a therapeutically active chimerical antibody against B-cell surface antigens. The chimerical antibody has a mouse V-region and a human C-region and is less immunogenic in humans than the corresponding murine antibody. See, for example, col. 1, line 2, and line. The chimerical antibody of Robinson et al., or any other prior art therapeutic chimerical antibody, is within the scope of instant claim 8, since the C-region of a human antibody is properly considered to constitute "a corresponding terminal portion of a homolog" of the mouse monoclonal antibody from which the chimerical antibody is engineered. Carr provides extrinsic evidence that the mouse C-region would inherently contain one or more T-cell epitopes. See, for

example, page 6, line 10 –page 7, line 4; page 10, lines 11-21; and page 13, lines 19-30.

Claims 9-10 are included because replacing the whole of a mouse antibody C-region with a human C-region would be expected to eliminate multiple T-cell epitopes.

Claim 7 is included because "having at least one amino acid substitution" is broad enough to encompass replacement of the whole murine C-region with a human C-region.

Claims 7-10 are rejected under 35 U.S.C. 102 (b) or (e) as being anticipated by Rodriguez et al. (EP 0,699,755, of record in IDS of 2/11/02, or corresponding U.S. 5,712,120).

Rodriguez et al's disclosure is similar to that of Carr. That is, T-cell epitopes within the framework segments of the V-region of a rodent antibody are modified by amino acid substitutions to render the V-region, non-immunogenic in humans. If one thus modifies a V-region rodent, C-region human chimerical antibody (e.g. claims 26-28 of Rodriguez et al. '755) one obtains the product of claim 7, assuming that the chimerical antibody is the "protein of interest". Additionally the chimerical antibody per se may be considered as a modification of a fully rodent antibody (the "protein of interest"), in which case claims 8-10 are anticipated, as argued supra regarding Robinson et al.

Claim 7 is rejected under 35 U.S.C. 102(b) as being anticipated by Barstad et al. (5,268,454).

Barstad et al teach analogs of a polypeptide immunogen which retains B-cell epitopes but which lacks T-cell epitopes. The latter are eliminated by chemical derivitization or are partially or completely deleted from the sequence. Applicant is referred to col.3, lines 55-66 and col. 4, lines 61-68.

It is to be noted that though Barstad et al teach the conjugation of the altered, T-cell epitope efficient polypeptide to a nonimmunogenic carrier polymer for the purpose of inducing B-cell energy (col. 2, line 58 –col. 3, line 3), the altered polypeptide, never the less, existed as a composition, per se, prior to its conjugation. This polypeptide would wherently be less immunogenic or nonimmunogenic, if injected into a host (applicant's own disclosure is relied upon for extrinsic evidence) and thus anticipates claim 7.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is (703) 308-3976. The examiner can normally be reached on Monday-Thursday 8 am - 5:30 pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Saunders/T.G.D.
January 2, 2003

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644